Role of ^{18}F-FDG PET/CT in the Assessment of Response to Antitubercular Chemotherapy and Identification of Treatment Endpoint in Patients With Tuberculosis of the Joints

A Pilot Study

Devansh Goyal, MS, Ravi Shriwastav, MS,† Ravi Mittal, MS,* Anshul Sharma, MD,‡ Vijay Sharma, MS,* Vijay D. Kumar, MS,* M.C. Sharma, MD,§ and Rakesh Kumar, MD, PhD||*

Aims: The aim of this study was to explore the utility of ^{18}F-FDG PET/CT in the assessment of response to antitubercular treatment (ATT) and identification of treatment endpoint.

Patients and Methods: Forty patients (mean age, 35.3 years; 27 men) with clinically, radiologically, and histopathologically proven joint tuberculosis prospectively underwent clinical, biochemical, and PET/CT evaluation at baseline and after ~6, 12, and 18 months of ATT. Two patients were lost to follow-up, and 1 defaulted treatment. The remaining 37 were followed up until complete response (CR) was achieved. Images were visually and quantitatively (SUV_{max} ratio and metabolically active disease volume [MV]) evaluated by 2 experienced nuclear medicine physicians.

Results: Knee (n = 18) and ankle (n = 7) were the most frequently involved sites. The median MV and SUV_{max} ratio at baseline were 85.10 mL and 7.21, respectively. Five patients had noncontiguous vertebral involvement, 12 had pulmonary lesions, 2 had abscesses, 6 had mediastinal, and 30 had local lymph nodal involvement. Complete response was seen in 1/39, 11/37, and 30/37 patients after 6, 12, and 18 months of ATT. Significant reductions in visual analog scale score, tenderness, joint swelling, SUV_{max} ratios, and MVs (Friedman test, $P < 0.001$) were seen after each follow-up. The median time-to-CR in skeletal lesions was significantly longer than extraskeletal lesions (591 vs 409 days; Wilcoxon signed-rank test, $P < 0.001$). Time-to-CR in joint lesions positively correlated with MV at first follow-up (Pearson = 0.452, $P = 0.005$) and negatively correlated with percentage change in MV (first follow-up from baseline) (Pearson = −0.620, $P < 0.001$). ROC analysis yielded a cutoff of ≤71% reduction in MV at first follow-up (80.8% sensitivity, 81.8% specificity) to predict extension of ATT beyond 12 months. Using ROC analysis at second follow-up, a cutoff of ≤12.67 mL (for CR) was derived and was validated in patients at the third follow-up, with an accuracy of 84.4%. Patients with CR in PET/CT maintained disease-free state during a mean follow-up of 271 days.

Conclusions: ^{18}F-FDG PET/CT is an excellent tool in estimating total disease burden, assessing response to ATT and identification of treatment endpoint in joint tuberculosis.

Key Words: PET/CT, ^{18}F-FDG, joint tuberculosis, ATT

(*Clin Nucl Med* 2021;00: 00–00)

Globally, approximately 10 million people are affected with tuberculosis every year.[1] Although pulmonary tuberculosis (PTB) is the most common presentation, extrapulmonary involvement (EPTB) is seen in approximately a fifth of the patients.[2–4] The proportion of EPTB has been increasing on account of a slower year-on-year decline in the number of EPTB patients, compared with PTB.[2] Approximately a tenth of the EPTB cases are composed of musculoskeletal involvement, with spine and big joints more often involved.[2,3,5] Although one may be able to find adequate literature on spinal tuberculosis,[6] the scarcity of prospective studies on extraspinal joint tuberculosis is evident. Because of this, among other things, there is still not enough literature available to generate consensus on the duration of antituberculosis treatment (ATT), which can range from 6 to 24 months.[5,7,8] CT, MRI, and ultrasonography are commonly used for the assessment of the lesion site. Among these, MRI is preferred for baseline evaluation (especially in the predestructive phase). However, its use in monitoring response to treatment is yet to be established as radiological changes can lag behind actual healing.[7,9] Direct evaluation of local metabolism using ^{18}F-FDG PET/CT can potentially avoid errors associated with reliance on these radiological changes. In recent literature, ^{18}F-FDG PET/CT has shown potential for response assessment in patients with spinal tuberculosis.[10]

The aims of this study were to evaluate the response to ATT using ^{18}F-FDG PET/CT and to identify an endpoint of the treatment in patients with extraspinal joint tuberculosis.

PATIENTS AND METHODS

Forty patients (mean age, 35 years; range, 14–64; 27 men) with clinically, radiologically, and/or histopathologically proven extraspinal musculoskeletal TB (with joint involvement) were prospectively recruited. Patients with a history of ATT intake, operated cases for TB (eg, synovectomy), known cases of multidrug-resistant TB, hypersensitivity to ATT, and those who refused to sign informed consent were excluded from the study. The patients were clinically assessed for signs and symptoms of musculoskeletal TB including pain, tenderness, and swelling of the affected part. Pain intensity was assessed using visual analog scale (VAS) score, a

Received for publication November 16, 2020; revision accepted December 9, 2020.
From the *Department of Orthopaedics, All India Institute of Medical Sciences, New Delhi, India; †Nepalgunj Medical College, Nepalgunj, Nepal; ‡Department of Nuclear Medicine, §Department of Pathology, and ||Diagnostic Division, Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India.
Study conducted in All India Institute of Medical Sciences, New Delhi, India.
Conflicts of interest and sources of funding: none declared.
Ethics approval: Ethical approval was obtained before initiation of the study.
Consent to participate: All patients signed the consent form.
Consent for publication: All authors have reviewed the final draft and consent to publications and journal's terms and conditions.
Availability of data and material: All the data can be made available upon request.
Compliance with ethical standards: None of the authors or their relatives have any conflicts of interest or any funding sources to disclose. Ethical clearance was obtained (reference IECPG-204, RT-4/28; September 28, 2017) from the ethical committee of our institute, before initiation of this study. This research involves human subjects. Written informed consent was taken from every subject in this study.
Correspondence to: Anshul Sharma, MD, Department of Nuclear Medicine, Raj Kumari Amrit Kaur OPD Complex, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029. E-mail: anshul.aiims@gmail.com.

ISSN: 0363-9762/21/0000–0000
DOI: 10.1097/RLU.0000000000003518

unidimensional measure of pain intensity, represented by a point between the extremes of "no pain at all" and "worst pain imaginable." It can be used as an optimal tool to describe the severity of pain because of its simplicity, reliability, and validity, as well as its ratio scale properties.[11,12] Degree of tenderness was assigned a score of 0 for no pain, 1 for mild pain, 2 for wincing, and 3 for withdrawal on palpation.[13] Joint swelling was scored as 0 for no swelling, 1 for mild, 2 for moderate, and 3 for filling of joint line.[13]

X-rays (anteroposterior and lateral views) and MRI of the affected part and blood investigations (complete blood cell count/renal function tests/liver function tests) along with inflammatory markers (erythrocyte sedimentation rate/C-reactive protein) were obtained. On the background of clinical-radiological diagnosis, biopsy was done, and the samples were sent for histopathology along with rapid culture sensitivity, Ziehl-Neelsen staining, GeneXpert, and polymerase chain reaction tests.

Before the start of ATT (2HRZE [isoniazid, rifampicin, pyrazinamide, ethambutol] + 16HRE), ^{18}F-FDG PET/CT was acquired to document the disease activity and extent of disease. Patients were followed at 6 months, 12 months, and 18 months of ATT using ^{18}F-FDG PET/CT. One patient was lost to follow-up by first follow-up, another by second follow-up, and 1 patient defaulted treatment before second follow-up. Among 37 patients, PET/CT could be acquired in 32 at the third follow-up. In patients, where ^{18}F-FDG PET/CT could not be acquired due to logistic difficulty (n = 5 at third follow-up), clinical, biochemical, and MRI evaluation were used instead to assess disease status. Four of these patients had already achieved complete response (CR) in PET/CT in the previous follow-up, and one who showed CR in MRI was followed up for another 6 months. By the end of the third follow-up, 7 patients still had residual disease in PET/CT. These patients were followed up with clinical, biochemical, and MRI evaluation, till CR was achieved and maintained. This was done due to ethical considerations (original ethical clearance was obtained for acquiring PET/CTs till third follow-up and to avoid subjecting these patients to additional radiation).

PET/CT Acquisition

PET scans were acquired on a dedicated PET/CT scanner (Biograph mCT; Siemens) (lutetium oxyorthosilicate [Lu_2SiO_5:Ce] detectors; attenuation coefficient, 0.89 cm^{-1}; photo fraction, 30%; decay constant, 40 ns; %FWHM of 10 and spatial resolution of 6 mm; paired to spiral CT [slice thickness, 4 mm; pitch, 1]; matrix of 512 × 512 pixels; and pixel size, ~1 mm). After fasting for at least 4 hours, ~5.3 MBq/kg of ^{18}F-FDG was intravenously injected. Scans were acquired after 60 minutes uptake period for 3 to 5 minutes/bed position, using a matrix of 128 × 128 pixels and slice thickness of 1.5 mm. Images were reconstructed using ordered subset expectation maximization (2 iterations and 8 subsets).

Interpretation of Image Findings

Two experienced nuclear medicine physicians independently evaluated the scans. Qualitative visual interpretation of images was used to assess response to therapy. The identification of resolution of disease was based on criteria and radiological characteristics detailed in the literature.[14,15] Partial response was diagnosed on the basis of reduction in uptake in the target lesion[16] and quantitative reduction of more than 30% in SUV (this was extrapolated from PERCIST [Positron Emission Tomography Response Criteria in Solid Tumors] criteria in oncology[17]). Similarly, increase in SUV_{max} of more than 30% was considered progressive disease.[17] This was done as SUV_{max} variation of ~20% to 30% can be due to measurement errors.[18]

For quantitation, the 3-dimensional regions of interest (ROIs) were drawn around the site of abnormal tracer uptake, and SUV_{max} was calculated according to the formula below:

$$\text{SUV} = \text{ROI activity (MBq/g)}/(\text{injected dose [MBq]}/\text{body weight [g]}).$$

Background ROIs were drawn over the ascending aorta (diameter, 10 mm).

RESULTS

Descriptive

Baseline ^{18}F-FDG PET/CT was acquired in all patients. Baseline characteristics in this population are detailed in Table 1.

Baseline ^{18}F-FDG PET/CT

All the involved joints showed increased ^{18}F-FDG uptake during the visual assessment, which was correctly identified by both nuclear medicine physicians. The median metabolically active disease volume (MV) was 85.10 mL (interquartile rate [IQR], 37.49–192.00), and the median SUV ratio was 7.21 (IQR, 4.35–13.82). MV did not show any relationship with VAS, tenderness score, or joint swelling (Kruskal-Wallis $P = 0.220$, 0.087, and 0.168, respectively). Although the differences were not statistically significant, MV was higher in patients with higher tenderness score (median of 126.00 mL in patients with a score of 3 vs 82.54 mL in those with a score 2) and joint swelling (medians 35.28, 65.84, and 116.00 in patients with scores 1, 2, and 3, respectively).

Similarly, SUV ratio did not show any relationship with VAS, tenderness score, or joint swelling (Kruskal-Wallis $P = 0.529$, 0.225, and 0.200, respectively). SUV_{max} ratios were similar in patients with tenderness scores of 3 and 2 (median, 7.61 vs 7.35). SUV_{max} ratios increased with the joint swelling (medians 4.25, 6.14, and 10.48 in patients with scores 1, 2, and 3, respectively).

Nonarticular Lesions

Five patients had noncontiguous vertebral involvement, 12 had pulmonary lesions, and 2 had abscesses (1 psoas and 1 gluteal). Lymph nodal involvement was seen in 36 patients. In 30, involved lymph nodes corresponded to the drainage area of the involved

TABLE 1. Baseline Characteristics in the Sample Population

Parameter	
Age	Mean, 35.3 years (range, 14–64)
Sex	27 men, 13 women
Body mass index, kg/m^2	Median, 21.5; IQR, 19.6–23.6
Baseline ESR	Median, 30.0; IQR, 23.8–41.2
Joints involved	Knee (n = 18), ankle (n = 7), foot (n = 6), wrist (n = 3), hip (n = 2), elbow (n = 2), sternoclavicular (n = 1), sacroiliac (n = 1)
VAS score for pain (0–10)	3 (n = 4), 4 (n = 7), 5 (n = 10), 6 (n = 12), 7 (n = 4), 8 (n = 2), 9 (n = 1)
Tenderness score (0 = no pain; 1 = mild pain; 2 = wincing; 3 = withdrawal on palpation)	1 (n = 1), 2 (n = 27), 3 (n = 12)
Joint swelling (0 = no swelling; 1 = mild; 2 = moderate; 3 = filling of joint line on account of swelling)	0 (n = 1), 1 (n = 3), 2 (n = 22), 3 (n = 14)

ESR, erythrocyte sedimentation rate.

TABLE 2. Quantitative Parameters at Baseline and First to Third Follow-ups

	Baseline	First Follow-up	Second Follow-up	Third Follow-up	*P* (Friedman Test*)
Time since recruitment, median (IQR), d	—	207 (167–234)	385 (363–417)	592 (552–659)	—
VAS, median (IQR)	5 (4–6)	2 (2–3)	1 (1–2)	1 (0–2)	<0.001
Tenderness, median (IQR)	2 (2–3)	1 (1–2)	1 (1–2)	0 (0–1)	<0.001
Joint swelling score, median (IQR)	2 (2–3)	1 (0–2)	0 (0–1)	0 (0–1)	<0.001
SUV_{max} ratio skeletal, median (IQR)	7.21 (4.35–3.82)	3.17 (2.24–4.30)	2.03 (1.40–2.97)	1.48 (1.02–2.01)	<0.001
SUV_{max} ratio extraskeletal, median (IQR)	5.22 (3.41–9.07)	1.76 (1.10–2.62)	1.15 (0.87–1.83)	1.11 (0.69–1.72)	<0.001
Metabolic volume, median (IQR)	85.10 (37.49–192.00)	31.65 (8.82–84.65)	17.12 (2.52–34.11)	7.30 (0.00–15.29)	<0.001

*Post hoc analysis with Wilcoxon signed-rank tests was conducted with a Bonferroni correction applied. $P < 0.05$ for all combinations).

joint. In 6, they were distant lymph nodes (mediastinal) with concomitant lung involvement seen in 2.

Follow-up Imaging

Changes in clinical scores and PET parameters with follow-up are given in Table 2. There was a significant reduction in pain, tenderness, and swelling and a significant concomitant reduction in the PET parameters during the period of treatment.

Response

Detailed breakups of the response of joint lesions to ATT are given in Figure 1. Patients with CR in PET/CT (n = 29) were followed up for median of 247 days (IQR, 117–355) with clinical, biochemical, and MRI evaluation. All these patients did not develop recurrence during the follow-up.

Time-to-CR

The median time-to-CR for skeletal lesions was 591 days (IQR, 417–661), and the median time-to-CR for extraskeletal lesions was 409 days (IQR, 299–633). The difference was statistically significant (Wilcoxon signed-rank test, $P < 0.001$). Rates of complete resolution at first, second, and third follow-up for skeletal lesions were 3%, 30%, and 78%, respectively, and for extraskeletal lesions were 28%, 57%, and 81%, respectively. Three of the cases with vertebral involvement showed resolution at the same time as the joint lesions, 1 preceded by ~6 months, and 1 delayed by the

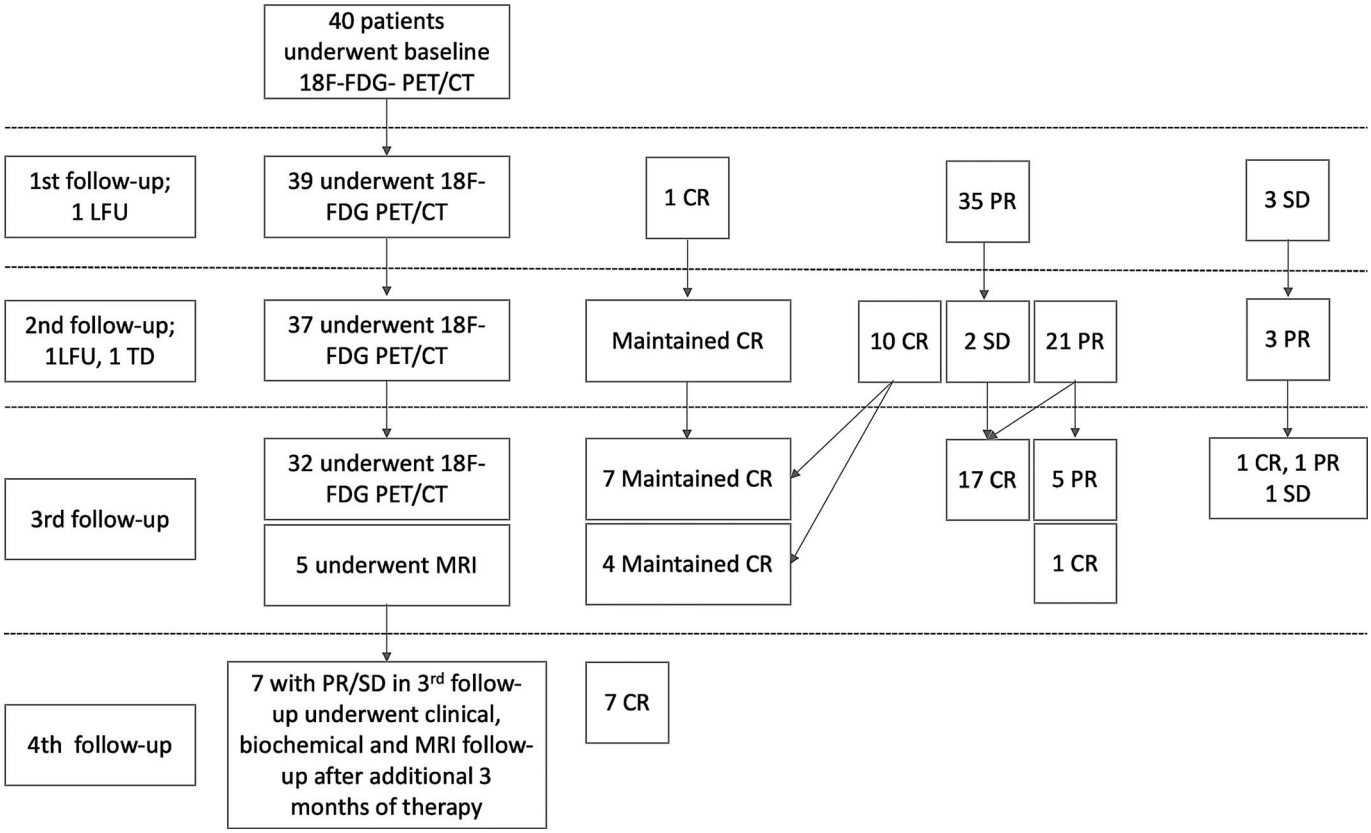

FIGURE 1. Flowchart depicting the patient follow-up and response evaluation in joint lesions (LFU indicates lost to follow-up; TD, treatment defaulted; PR, partial response; SD, stable disease). Note: at the third follow-up, 1 patient with SD, 1 with CR, and 4 with PR in joint lesions also had a residual low-burden extraskeletal disease. All of these lesions were resolved by the fourth follow-up.

same amount. In 1 patient, resolution of extraskeletal lesions lagged by more than 6 months.

Patient age and BMI were not significant between the patients who showed CR at second and third follow-up versus those with residual disease (Mann-Whitney *P* values for "age" at second and third follow-up of 0.148 and 0.767, respectively; and for "BMI," 0.273 and 0.632, respectively). Baseline MTV, SUV in skeletal lesions, SUV in extraskeletal lesions, time-to-CR in skeletal lesions, and time-to-CR in extraskeletal lesions showed no significant correlation with age or BMI (*P* values for age: 0.386, 0.564, 0.132, 0.153, and 0.275; for BMI: 0.933, 0.968, 0.291, 0.147, and 0.423). Similarly, baseline MTV, SUV in skeletal lesions, SUV in extraskeletal lesions, time-to-CR in skeletal lesions, and time-to-CR in extraskeletal lesions were not significantly different between men and women (Mann-Whitney, $P = 0.081$, 0.220, 0.740, 0.529, and 0.184, respectively).

Time-to-CR in joint lesions positively correlated with the MV at first follow-up (Pearson = 0.452, $P = 0.005$) and negatively correlated with the percentage change in MV at first follow-up (Pearson = −0.620, $P < 0.001$). However, no significant correlation was seen with baseline MV ($P = 0.362$), SUV ratio ($P = 0.748$), change in SUV at first follow-up ($P = 0.218$), and other parameters.

ROC analysis was performed to predict patients who would require prolongation of therapy beyond 12 months. A reduction of ≤71% in MV in first follow-up PET/CT (from baseline) predicted the same, with sensitivity of 80.8% and specificity of 81.8% (area under the curve, 0.899; 95% confidence interval [CI], 0.787–1.000; $P < 0.001$). The odds ratio for prolongation of therapy in patients the MV reduction ≤71% at first follow-up was 18.90 (3.07–116.21) (Figs. 2, 3).

Quantitative Treatment Endpoint

Images were analyzed both qualitatively and quantitatively for response. We also tried to determine a quantitative cutoff for the diagnosis of a CR. At the second follow-up, 11 patients showed CR. They were followed up for a median of 279 days (IQR, 235–361), and none developed recurrence.

Although median SUV_{max} ratio in patients with CR was lower (1.87 [IQR, 1.46–2.43] vs 2.08 [IQR, 1.34–4.11]), the difference was not significant (Mann-Whitney $P = 0.288$).

MV in patients with CR was significantly lower (2.00 mL [IQR, 0.00–3.43] vs 22.10 mL [IQR, 14.16–47.88]; Mann-Whitney $P < 0.001$). Using ROC analysis, we obtained an area under the curve of 0.897 (95% CI, 0.789–1.000) and a cutoff of ≤12.67 mL for CR (90.9% sensitivity and 80.8% specificity). We validated this cutoff in patients at the third follow-up and were able to predict CR with a sensitivity of 84.0% (95% CI, 65.3–93.6), specificity of 85.7% (48.7–97.4), positive predictive value of 95.4% (78.2–99.2), negative predictive value of 60.0% (31.3–83.2), and accuracy of 84.4% (68.2–93.1).

At the third follow-up, among 32 patients who underwent PET/CT, 1 had shown complete resolution at first follow-up, 6 at second follow-up, and 18 at the third follow-up. Seven patients still showed residual disease.

At third follow-up, there was a significant difference between the median SUV_{max} ratios of the patients who showed residual disease (n = 7) and those who had shown CR 6 months earlier (and underwent follow-up scan 6 months later; n = 6) (Mann-Whitney, $P = 0.032$). However, there was no significant difference in SUV_{max} ratios between the patients who showed residual disease at the third follow-up (n = 7) and those who showed complete resolution for the

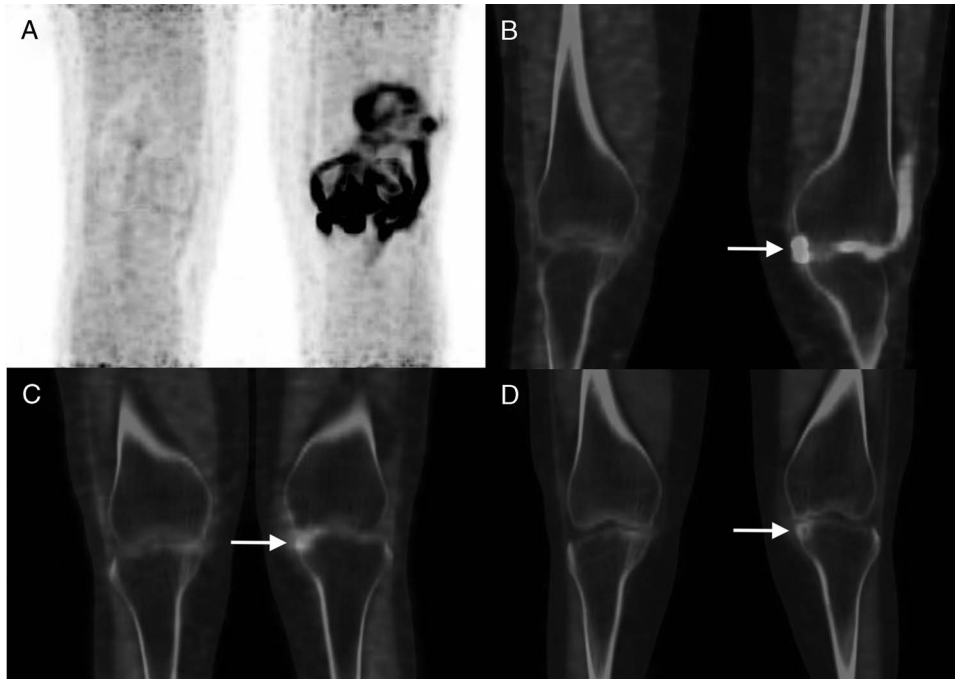

FIGURE 2. ^{18}F-FDG PET/CT in a 32-year-old woman, with tubercular involvement of the left knee joint. **A**, MIP image showing the extent of the disease at baseline. **B**, Coronal images (baseline) showing increased tracer uptake (arrow) involving the knee joint space and synovium. **C**, Coronal images (after 6 months of ATT) showing significant reduction in the extent of disease (note the decrease in the area with increased ^{18}F-FDG uptake). **D**, Coronal images (after 12 months of ATT) showing minimal ^{18}F-FDG uptake at the medial condyle of the tibia (arrow), with appearance of sclerosis. This residual uptake is due to the reactive/healing process.

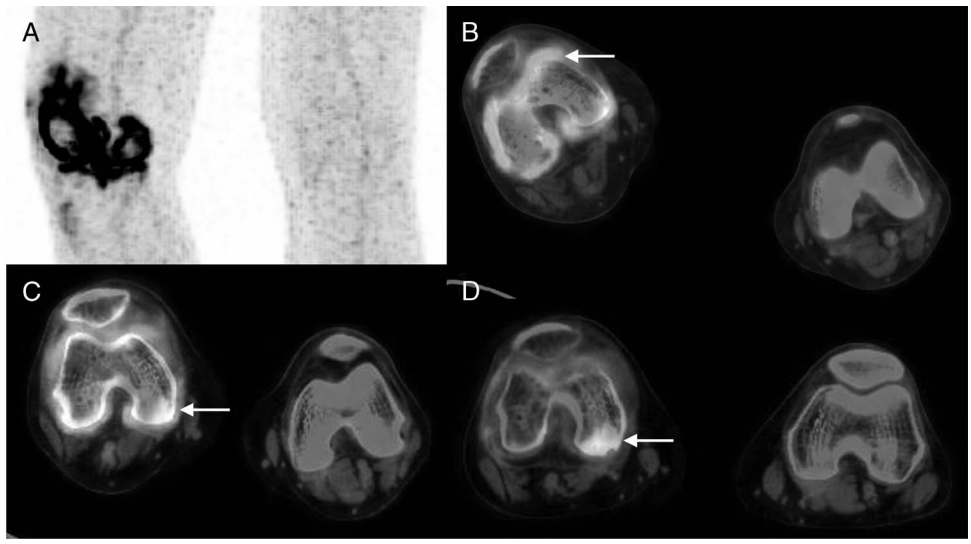

FIGURE 3. ^{18}F-FDG PET/CT in a 30-year-old man with tubercular involvement of the right knee joint. **A**, MIP image showing the extent of the disease at baseline. **B**, Axial images (baseline) showing increased tracer uptake involving the right knee joint space and the synovium (arrow). **C**, Axial images (after 6 months) showing no significant decrease in the extent of disease. **D**, Axial images (after 18 months) showing residual minimal disease in the synovium as well as the medial condyle of the femur (arrow).

first time at the third follow-up (Mann-Whitney, n = 18) ($P = 0.333$). This showed that SUV_{max} ratios lagged behind the MV by approximately 6 months in showing significant reduction in patients with CR.

DISCUSSION

Musculoskeletal tuberculosis is a relatively rare manifestation of tuberculosis. The involvement of joints is even rarer. In a retrospective study, bone and joint tuberculosis was seen in only 3.6% of the patients, with less than half of them showing of nonspinal involvement.[19] Due to the relative rarity of joint TB, there are not many prospective studies, to build a consensus on the duration of therapy.[5,7,8] Because there can be a disconnect between the rate of structural resolution and the healing process,[7,9] direct imaging of the metabolism with ^{18}F-FDG can provide the way forward. ^{18}F-FDG is a glucose analog that is not metabolized after the first phosphorylation and is therefore trapped inside the cells. It has been shown to have a role in diagnosis and monitoring the treatment in infectious and inflammatory diseases, based on local metabolism as measured by SUV_{max}.[20,21] Reduction in SUV_{max} has also been documented with the continuation of treatment in tuberculosis patients,[9,10] and this reduction was shown to correlate with functional improvement.[10]

In our study, the mean age was 35 years, with male preponderance, which is in agreement with the latest epidemiological data from World Health Organization[1] and studies in patients with bone and joint tuberculosis.[8,22] Only approximately 50% of patients had a VAS score of more than 5; however, on examination, most patients had joint tenderness and swelling. This is in contrast to another study,[10] where almost all patients had VAS of 6 and above. This might be on account of the site of involvement as the quoted study was conducted in patients with spinal tuberculosis, which often presents with pain and neurological symptoms. A small number of patients with hip infections was on account of our selection criterion, where histological confirmation was needed to diagnose tuberculosis. Therefore, more accessible joints were more frequent.

Active pulmonary involvement was seen in 30% of the patients and multifocal bone involvement in 12.5%. Both statistics are in line with the reported literature.[8,22] However, lymph nodal involvement was much higher. If we were to ignore lymph nodes in the drainage area of the involved joints and those seen with active PTB, only 4 cases remain. Therefore, high incidence of lymph nodal involvement in our study was likely on account of local extension. In fact, destructive lytic lesions with surrounding soft tissue involvement were a feature in these patients.

There was a significant reduction in the SUV_{max} ratio and metabolic volumes in the skeletal lesions, which was paralleled by the reduction in VAS score, tenderness, and joint swelling. Although clinical scores had practically normalized by the first follow-up, only 1 patient showed CR. However, more than 50% reduction was seen in SUV_{max} ratios and metabolic volumes. This reduction in inflammatory volumes might have been responsible for the alleviation of symptoms. Reduction in SUV_{max} to nearly half within 6 months is consistent with other studies.[10,23] The absolute values seem smaller because we used ratios instead of absolute SUV_{max}. The use of these ratios allowed us to normalize SUV_{max} values to the background activity. This was done to reduce errors in the measurement of SUV_{max} on account of the patient's physiological makeup.[24,25]

What is more intriguing was our findings with metabolic volumes. Although measurements of metabolic volumes are commonplace in oncological imaging, to our knowledge, this is the first instance of their use in patients with tuberculosis. Metabolic volumes are different from structural volumes, as they only measure the metabolically active (^{18}F-FDG avid) component of the disease. The reduction in metabolic volumes was more marked than the reduction in SUV_{max}. MVs and not SUV_{max} ratios correlated with time-to-CR. A much stronger negative correlation was seen with the percentage change in MV at the first follow-up. This was likely because our study sample consisted of both small and big joints. Using percentage change allowed us to normalize these variations. Through ROC analysis, ≤71% reduction in MVs at first follow-up (~6 months) was found to predict patients requiring therapy beyond 12 months. We also derived and validated a cutoff of ≤12 mL

(approximately) as a marker of CR, achieving ~84% diagnostic accuracy. This residual metabolic volume (less than 12 mL) was most likely a result of reactive/healing-associated changes, which may be seen months after resolution of the active disease.[26] In fact, this was the very reason we used both qualitative and quantitative analysis of PET/CT images. This is in line with another study[15] where visual analysis showed the best results in differentiating infected form noninfected nonunions. Radiographic features of active osteomyelitis and healing-associated changes were also used to further reduce false-negatives.[14] Another interesting finding was that SUV_{max} ratios lagged behind MTV, by ~6 months, when it became low enough to show a significant difference between CR and PR. This again proves the robustness of using MV to determine treatment endpoint.

Although most literature reports the use of 6 to 12 months of chemotherapy in patients with nonresistant tuberculosis, in our study, only ~30% of patients showed CR at 12 months. Interestingly, 4 of the 5 vertebral lesions had resolved by 12 months. In fact, ~30 mL of residual MV was seen in the unresolved articular lesions at 12 months, along with qualitative findings such as osteolysis, tissue destruction, and soft tissue involvement. Prolongation of ATT by 6 months increased the resolution rate to ~80%. Healing was marked by a reduction in SUV_{max} ratios and metabolic volumes, appearance of sclerosis, and resolution of soft tissue component (and uptake). In addition, none of the patients who were diagnosed as having CR in PET/CT developed recurrence when followed up for ~9 to 10 months with MRI, clinical, and biochemical evaluation. After ~18 months of chemotherapy, 7 patients still showed residual disease (with MV, ~30 mL). Six of them also had unresolved extraskeletal lesions. They developed CR with continuation of ATT for another 3 months. Although we did not see any significant difference in terms of patient characteristics such as age, sex, or BMI, bacterial characteristics might have been responsible for the delayed response (in both skeletal and extraskeletal lesions) in these patients. We did not obtain bacterial burden or sensitivity testing at each follow-up. Although this would have added to the quality of the data and allowed us to better differentiate the reactive changes from infective disease, additional invasive procedures would have been needed, with increasing likelihood of procedure-related complications. However, due to the continued response to ATT in all these patients, a reasonable assumption may be made that none of the patients developed any significant resistance. Still, this was a limitation of this study, which may be addressed with future trials.

In patients, who underwent additional PET/CT after the CR and discontinuation of therapy, further reduction of SUV_{max} ratios and MVs was noted. This was likely on account of healing and resolution of reactive changes. Almost all had MVs less than 12 mL.

In this study, we were able to prove the feasibility of ^{18}F-FDG PET/CT in quantifying disease burden, in monitoring treatment response, and in identifying quantitative endpoint to ATT using metabolic volumes in patients with osteoarticular tuberculosis. Finally, we were able to predict the need for prolongation of ATT beyond 12 months, using the percentage change in metabolic volumes at the first follow-up.

The use of prospective study design, qualitative and quantitative evaluation, and robust follow-up is the strength of this study. The drawbacks include the absence of head-to-head comparison with MRI at follow-ups. This was done to reduce inconvenience to the patients and to reduce the complexity and cost of the study. We do plan to compare MRI and PET/CT in a future study, in patients with active disease admixed with healing and arthritic changes. Finally, extrapolation of PERCIST criteria for response assessment in infections was based on the fact that ~25% variation in SUV values between sequential scans may be seen on account of measurement errors, which are independent of oncological versus nononcological indications.[18] Still, these criteria were not designed for infectious diseases, and therefore we verified our results by correlating quantitative response with qualitative radiological criteria.

CONCLUSIONS

^{18}F-FDG PET/CT is an excellent tool in the estimation of total disease burden, assessment of response to treatment, and identification of treatment endpoint in osteoarticular tuberculosis. Quantification of early response in ^{18}F-FDG PET/CT can predict the need for prolonged treatment in these patients. In the treatment of extraspinal joint tuberculosis, prolongation of ATT till 18 months is often required.

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